REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at 858 720 5133.

Status of the Claims

Pending claims

Claims 1 to 11, 13 to 21 and 31 to 44 are pending.

Claims added in the instant amendment

In the present response, new claims 45 to 52 added. Accordingly, after entry of the instant amendment, claims 1 to 11, 13 to 21 and 31 to 52 will be pending and under examination.

Allowed claims

Applicants thank the Examiner for finding claims 1 and 2 allowable.

Outstanding Objections and Rejections

Claims 5 to 9 and 21 are objected to for informalities. Claims 15 to 17, 20, 21 and 41 to 43 are rejected under 35 U.S.C. §112, first paragraph.

Applicants respectfully traverse all outstanding objections to the specification and claims and rejections of the claims.

Claim Objections

Claims 5 to 9 and 21 are objected to for informalities. The instant amendment addresses this issue.

Support for the Claim Amendments

Support for the claim amendments can be found throughout the specification. Accordingly, Applicants respectfully submit that no new matter is introduced by the instant amendments.

Issues under 35 U.S.C. §112, first paragraph

Claims 15 to 17, 20, 21 and 41 to 43 are rejected under 35 U.S.C. §112, first paragraph.

Written Description

Claims 15 to 17 are rejected under 35 USC §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

Claim 15 is directed to polynucleotides having a length of at least 15 nucleotides, wherein the nucleotides are contiguous bases of a polynucleotide encoding the exemplary polypeptide SEQ ID NO:28, and their complement sequences, and the polynucleotides hybridize with specificity to a polynucleotide that encodes a phosphatase or hybridizes with specificity to complementary sequences, or hybridize with specificity to a nucleic acid encoding an enzymatically active fragment of the phosphatase, under specific hybridization conditions.

Claim 16 is directed to polynucleotides having a length of at least 15 nucleotides, wherein the nucleotides are contiguous bases of polynucleotides that encode a polypeptide having at least 70% sequence identity to the exemplary SEQ ID NO:28 or enzymatically active fragments thereof, and their complementary sequences, and hybridize with specificity to complementary sequences, and the polynucleotides hybridize with specificity to a polynucleotide that encodes a phosphatase, or hybridize with specificity to a nucleic acid encoding an enzymatically active fragment of the phosphatase, or its complement, under specific hybridization conditions.

Claim 17 is directed to polynucleotides having a length of at least 15 nucleotides, wherein the nucleotides are contiguous bases of polynucleotides having phosphatase activity and having at least 70% sequence identity to a polynucleotide encoding an enzyme having phosphatase activity contained in ATCC Deposit No. 97379, or enzymatically active fragments thereof, and the polynucleotides hybridize with specificity to a polynucleotide that encodes a polypeptide that has phosphatase activity or hybridizes with specificity to its complementary sequence, under specific hybridization conditions.

As discussed, inter alia, on page 4, second full paragraph, of the instant office action (see, e.g., lines 11 to 12), the Patent Office is concerned that the pending claims may be directed to a genus of functionally unrelated polynucleotides. However, Applicants respectfully note that all claimed nucleic acids either encode an enzyme having phosphatase activity or enzymatically active fragments thereof, or, can be used to identify nucleic acids encoding a polypeptides having phosphatase activity, i.e., can hybridize under specific conditions to an enzyme having phosphatase activity or enzymatically active fragments thereof.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification such that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully submit that describing a genus of polynucleotides in terms of physico-chemical properties (e.g., a % sequence identity or stringent hybridization to the exemplary SEQ ID NO:19 or nucleic acids encoding SEQ ID NO:28) and function (e.g., encoding a polypeptide having phosphatase activity) satisfies the written description requirement of section 112, first paragraph.

As declared by Dr. Short (please see attached Rule 132 declaration, who was an expert in the field of molecular biology and enzyme development at the time of the invention), procedures for identifying nucleic acids that encode enzymes such as phosphatases were conventional and routine in the art at the time of the invention. Dr. Short declares that procedures for identifying polypeptides having phosphatase activity were conventional and routine in the art at the time of the invention. An exemplary assay for identifying polypeptides having phosphatase activity is described, inter alia, in the paragraph spanning pages 39 and 40 of the WO 97/48416 specification. Dr. Short declares that one of ordinary skill in the art using the teaching of the specification could have made and expressed nucleic acids having a percent sequence identity to an exemplary nucleic acid, or, which hybridized under defined conditions to an exemplary nucleic acid, and using routine screening could have determined with predicable positive results which of those nucleic acids encoded a polypeptide having phosphatase activity. Thus, Dr. Short declares that using the teaching of the specification one of ordinary skill in the art would be able to ascertain the scope of the claimed genus of phosphatases and phosphatase-

encoding nucleic acids with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing.

Dr. Short also declares that one of ordinary skill in the art using the teaching of the specification would have been able to make nucleic acids that encode for fragments of the exemplary phosphatase-encoding nucleic acid and express those nucleic acids, and using routine screening determine with predicable positive results which of the identified nucleic acids encode polypeptides having phosphatase activity. Dr. Short declares that one of ordinary skill in the art using the teaching of the specification would have been able to ascertain what fragments of the exemplary nucleic acid could be used to identify phosphatase-encoding nucleic acids. Dr. Short declares that one of ordinary skill in the art using the teaching of the specification would have been able to ascertain what fragments of the exemplary phosphatase could be used to identify enzymatically active fragments. Thus, Dr. Short declares that using the teaching of the specification one of ordinary skill in the art would be able to ascertain the scope of the claimed genus of phosphatases and phosphatase-identifying nucleic acids with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing.

The Patent Office alleges that species of nucleic acids encompassed by SEQ ID NO:19 is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus (please note, e.g., the lines 12 to 17, of page 4 of the office action).

Applicants respectfully aver that the described phosphatase nucleic acid and polypeptide species of the invention are sufficient to put one of skill in the art in possession of the attributes and features of all species within the genus of claimed nucleic acids and polypeptides of the invention. In fact, both the Patent Office and the Federal Circuit set forth conditions where a single species is sufficient to put one of skill in the art in possession of the attributes and features of all species within a genus, where the genus is defined in terms of shared physical and structural properties with the single species.

Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph, and note that the guidelines state that a description of a genus of polynucleotides in terms of its physico-chemical properties, e.g., a % sequence identity, to a single exemplary species, and a common function

satisfies the written description requirement of section 112, first paragraph, for the genus of polynucleotides.

In Example 14 of the Guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of Example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the genus of nucleic acids and polypeptides of the invention are described by structure (the exemplary SEQ ID NO:19 or encoding SEQ ID NO:28), a physico-chemical property (a percent sequence identity or stringent hybridization to SEQ ID NO:19 or nucleic acids encoding SEQ ID NO:28) and function (having phosphatase activity). All species of the claimed genus must have a percent sequence identity to an exemplary sequence (e.g., SEQ ID NO:19, nucleic acids encoding SEQ ID NO:28, or SEQ ID NO:28). The USPTO guidelines recognize that written description is met for a genus of nucleic acids or polypeptides described by a structure, a physico-chemical property (e.g., a % sequence identity) and a defined function, the genus of claimed nucleic acids or polypeptides also meet the written description requirements of section 112.

The genus of nucleic acids or polypeptides of the invention also fully comply with the requirements for written description of a genus of nucleic acids as set forth, inter alia, in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the*

members of the genus, which features constitute a substantial portion of the genus." (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of phosphatase-encoding nucleic acids and phosphatases of the invention. In one aspect, the claimed genus of nucleic acids and phosphatases all must have phosphatase activity and a specific physical characteristic, e.g., a % sequence identity to an exemplary nucleic acid or polypeptide (e.g., SEQ ID NO:19, nucleic acids encoding SEQ ID NO:28, or SEQ ID NO:28). Therefore, the claimed genus of phosphatases and phosphatase-encoding nucleic acids is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

Similarly, in this court's most recent pronouncement, it noted:

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the function of claimed phosphatases or phosphatase-encoding or phosphatase-identifying nucleic acids is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity or stringent hybridization). Accordingly, the sequences of the invention are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirements under 35 U.S.C. §112, first paragraph. In light of the above

remarks, Applicants respectfully submit that claimed invention is sufficiently described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Enablement

Claims 3 to 5, 10, 11, 13 to 21 and 31 to 44 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Patent Office states that the specification is enabling for polynucleotides which encode the amino acid sequence of SEQ ID NO:28 or enzymatically active fragments thereof.

However, it is alleged that the specification does not reasonably provide enablement for the claimed genus of nucleic acids, e.g., those that hybridize under stringent conditions to the exemplary nucleic acid or those that have a percent sequence identity to the exemplary nucleic acid of the invention. It is alleged, inter alia, that predictability of which changes can be tolerated in a protein's amino acid sequence and obtain a desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification. It is alleged that it would have required some knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues or tertiary structure, that correlate with phosphatase activity to generate the claimed genus of polypeptide-encoding nucleic acids without undue experimentation.

Applicants respectfully aver that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, the genus of phosphatase-encoding nucleic acids and phosphatases of the claimed invention. In support, Applicants submit for consideration a Rule 132 declaration by Dr. Jay Short, who was an expert in the field of molecular biology and enzyme development at the time of the invention.

Dr. Short declares that procedures for modifying and expressing nucleic acids were conventional and routine in the art at the time of the invention. Dr. Short declares that procedures for determining the activity of the expressed modified nucleic acids and determining if the nucleic acids expressed a polypeptide with phosphatase activity were conventional and routine in the art at the time of the invention. Dr. Short declares that procedures for determining

sequence identity to an exemplary nucleic acid or whether a nucleic acid hybridized to a target nucleic acid under defined conditions were routine in the art at the time of the invention. Dr. Short declares that procedures for expressing and screening for phosphatase activity were conventional and routine in the art at the time of the invention.

Dr. Short declares that one of ordinary skill in the art using the teaching of the specification would have been able to make phosphatase-encoding nucleic acids having at least 70% sequence identity to the exemplary nucleic acid, or phosphatase-encoding nucleic acids that hybridize under defined hybridization conditions to the exemplary nucleic acid, to make and use the genus of compositions of the invention without undue experimentation. Dr. Short declares that it was considered routine by one skilled in the art at the time of the invention to screen for multiple substitutions or modifications of a nucleic acid or a polypeptide for functional variations, including screening for a genus of phosphatase-encoding nucleic acids or a genus of phosphatases. Dr. Short declares that it was considered routine by one skilled in the art at the time of the invention to screen for subsequences of nucleic acids that encode enzymatically active fragments of an exemplary enzyme. Dr. Short declares that it was considered routine by one skilled in the art at the time of the invention to screen for subsequences of nucleic acids that can identify by hybridization a phosphatase-encoding nucleic acid. For example, high throughput methods for screening for enzyme activity, such as phosphatase activity, were well known in the art. Dr. Short declares that while the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (e.g., finding a genus of nucleic acids encoding phosphatases) predictable. Accordingly, Dr. Short declares that at the time of the invention it would have been considered routine by one skilled in the art to generate and screen multiple substitutions or multiple modifications in an exemplary nucleic acid sequence and predictably generate a genus of phosphatase-encoding nucleic acids or a genus of phosphatases.

Dr. Short declares that it was not necessary for the skilled artisan to understand which specific regions of phosphatase sequence or structure needed to be modified without affecting function or activity to routinely generate the claimed genus of phosphatase-encoding nucleic acids. Dr. Short declares that methods for sequence modifications were sufficiently comprehensive, routine and predictable at the time of the invention to predictably generate

phosphatase-encoding sequences without need of knowing which specific regions of phosphatase sequence or structure affected phosphatase function or activity. Dr. Short declares that methods known at the time of the invention for modifying nucleic acid sequences in combination with high through-put enzyme activity screening known at the time of the invention, made methods that require previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary. Accordingly, Dr. Short declares that using methods known in the art at the time of the invention, it would not have been necessary to understand which specific regions of phosphatase structure needed to be modified to generate a genus of nucleic acids or polypeptides for practicing the invention without undue experimentation.

Dr. Short declares that the specification provides sufficient guidance to one of ordinary skill in the art as to whether a nucleic acid or polypeptide falls within the scope of the claimed genus. Dr. Short declares that methods for determining the requisite structure (sequence based on percent sequence identity to an exemplary nucleic acid or polypeptide) and function (phosphatase activity) are clearly set forth in the specification. Dr. Short declares that at the time of the invention, high through-put *in vivo* (e.g., whole cell) nucleic acid expression and enzyme activity screening protocols were well known in the art. The specification sets forth an exemplary phosphatase screening assay to determine if a nucleic acid or polypeptide is within the scope of the claimed genus, inter alia, in the paragraph spanning pages 39 and 40 of the WO 97/48416 specification. Dr. Short declares that methods for determining sequence identity were also routine and well known in the art at the time of the invention. Dr. Short declares that while the numbers of alternative species that needed to be screened may have been high, the protocols for screening were routine and positive results predictable. Accordingly, the specification provided sufficient guidance to one of ordinary skill in the art to make and use the claimed genus of nucleic acids or polypeptides to practice the invention.

Whether large numbers of compositions (e.g., nucleic acids, enzymes, antibodies, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the

enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognized the need to screen numbers of negatives to find a sample that has the desired properties, e.g., phosphatase-encoding activity, or, the ability to identify by hybridization a phosphatase-encoding nucleic acid, or a polypeptide having phosphatase activity. Furthermore, as declared by Dr. Short, methods of making and screening procedures used to identify nucleic acids and polypeptides of the claimed invention were all well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could have practiced the instant claimed invention without undue experimentation.

Applicants respectfully submit that the pending claims meet the enablement requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that the specification sufficiently described how to make and use the claimed methods to satisfy the requirements of 35 U.S.C. §112, first paragraph.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first paragraph. Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 720 5133.

Respectfully submitted,

Date: May 18, 2004

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